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Prevalence of Antibodies to HTLV in Antenatal Clinic Attenders in South East London

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The prevalence of antibodies to HTLV in women attending a south east London antenatal clinic between October 1990 and July 1992 was determined using sera referred for routine rubella antibody testing. Samples were screened for HTLV antibody using a modified Fujirebio gel particle agglutination test and reactive sera confirmed by ELISA (Abbott Laboratories, North Chicago, IL) and two commercial Western blots (Cambridge Biotech Inc., Rockville, MD, and Diagnostic Biotechnology, Genelab Diagnostics, Louvaine, Belgium). This strategy confirmed the presence of HTLV-1 antibodies in 12 out of 6,289 sera (0.19%, 95% confidence limits 0.083% to 0.30%) and HTLV-2 antibodies in 2 (0.03%) sera. Specimens from 8 of 821 (0.97%, 95% confidence limits 0.42% to 1.9%) Afro-Caribbean women, three of 1,136 (0.26%, 95% confidence limits 0.055% to 0.78%) African women, and one of 3,049 (0.033%, 95% confidence limits 0.006% to 0.18%) Caucasian women were positive for HTLV-1 antibodies. Sera from Afro-Caribbean women born in the Caribbean were 7.6 times more likely to be HTLV-1 antibody positive than sera from Afro-Caribbean women born in the UK (P = 0.012). Selective testing of Afro-Caribbean and African antenatal clinic attenders, in this setting, would have identified 11 of the 12 HTLV-1 infections at an estimated cost of prevention of HTLV-1 associated disease of £100,000 per case which is considerably less than the £1.3 million which has been estimated to prevent a case by universal screening of UK blood donors. ***J. Med. Virol. 52:326–329, 1997.***

KEY WORDS: epidemiology; ethnicity; diagnosis; screening test

INTRODUCTION

Human T-cell leukaemia/lymphoma virus types 1 and 2 (HTLV-1 and HTLV-2) are retroviruses which cause persistent infection in CD4 positive lymphocytes. A healthy carrier state follows asymptomatic primary infection with a proportion of infected individuals later developing adult T-cell leukaemia/lymphoma (ATL) or tropical spastic paraparesis (TSP, also known as HTLV-associated myelopathy). The pathogenesis of ATL and TSP is largely unknown, but the life-time risk of developing disease has been estimated to be between 1 in 20 and 1 in 50 for ATL and about 1 in 400 for TSP [Murphy et al., 1989; Kaplan et al., 1990]. No definite disease association has been shown for HTLV-2.

HTLV-1 can be transmitted sexually, by blood products containing white blood cells, by sharing intravenous needles, and from mother to infant, primarily via breast milk [Kusuharah et al., 1987]. In regions of Japan with high HTLV-1 carriage rates antenatal women are screened for HTLV-1 and seropositive women are advised not to breast feed. This single measure is able to reduce mother to child transmission by 80% [Oki et al., 1992].

HTLV-1 is endemic worldwide but has a relatively high endemicity in Southern Japan, the Caribbean islands, and parts of South America and Africa. The prevalence of HTLV-1 in UK blood donors is very low and four of the five HTLV-1 seropositive donors identified in a recent survey had an identifiable risk factor of sexual contact with an Afro-Caribbean partner [Brennan et al., 1993]. In the US, about 25 to 30% of sexual partners of HTLV-1 seropositive blood donors are also seropositive [Anon, 1993]. Thus the largest group in the UK at risk of HTLV-1 carriage are Afro-Caribbeans and their partners [Simms et al., 1994].

A previous report based on a small number of families suggested that HTLV-1 seropositivity was less common in Afro-Caribbeans born in the UK than in those born in the Caribbean [Cruikshank et al., 1990]. This trend was also observed in a recent study of antenatal attenders in Birmingham where two of 78 Afro-Caribbean women born in the Caribbean were HTLV-1 positive in contrast to none of 408 Afro-Caribbeans born in the UK [Nightingale et al., 1993].

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TABLE I. Recorded Ethnicity of Antenatal Clinic Attenders (6,281 Sera)*

Ethnicity	Birth place					Total
	UK	Africa	Caribbean	Other	N/K	
Caucasian	2,845	20	7	145	32	3,049 (54%)
African	170	925	1	3	37	1,136 (20%)
Afro-Caribbean	596	3	194	13	15	821 (15%)
Others[a]	244	23	6	354	23	650 (11%)
Total	3,855	971	208	515	107	5,656

*No data available on 625 sera (10% of all samples tested for HTLV antibodies).
[a]Include Asian (India, Pakistan, Bangladesh, and south east Asia), Japanese, and Chinese.

We now report the results of an unlinked anonymous study of HTLV in antenatal clinic attenders in south east London in an area where Afro-Caribbean and African women form a high proportion of clinic attenders. Sera obtained for routine testing of rubella antibody was used to measure the prevalence of HTLV antibody and identify possible risk factors of ethnicity, including the birth place of the clinic attender, and also the ethnicity of their partner. Information was not recorded on past history of intravenous drug abuse.

METHODS

Between October 1990 and July 1992 sera referred for rubella testing from antenatal clinic attenders were tested for HTLV antibodies in a modified Fujirebio gel particle agglutination test. All specimens containing sufficient sera for testing were included in the study. The assay was similar to that used by others [Barbara et al., 1989; Cossen et al., 1992], with the exception that sera were tested at a dilution of one in 30 and gel particles were used at a dilution of one in 10, both in phosphate buffered saline (pH 7.2) with the addition of 0.05% Tween 20. The sensitivity of the assay had been evaluated using a panel of HTLV-1 positive sera from asymptomatic patients and patients ATL (data not shown). Sera reactive in this assay were tested in a commercial ELISA (Abbott Laboratories) in accordance with the manufacturers instructions. Sera positive in the ELISA were then tested in two commercial Western Blot assays following the manufacturers' directions (Cambridge Biotech and Diagnostic Biotechnology) to confirm the presence of HTLV antibodies and to discriminate between HTLV-1 and HTLV-2 infections. Demographic information of antenatal attenders were taken from the antenatal booking records. All sera were anonymised prior to testing for HTLV antibodies and permission for the study had been given by the Ethical Committee of King's College Hospital. Confidence intervals were calculated using Confidence Interval Analysis (CIA Ver 1, Prof. MJ Gardner and B.M.J.) and relative risks using EPI Info Ver 6 (CDC and WHO) using 2 × 2 tables and Fisher's exact test.

RESULTS

Sera from 6,281 antenatal clinic attenders submitted for routine testing of rubella antibody were tested for HTLV antibody. Ethnicity data was available for 5,656 women (90%), with Afro-Caribbean women constituting the third largest group after Caucasian and African women (Table I). Two hundred and thirty seven sera (3.8%) were positive in the modified gel particle agglutination test of which 21 were positive in the ELISA. Fourteen sera were confirmed positive in the Cambridge Biotech Western blot assay with 12 positive for HTLV-1 antibody (Table II) and two positive for HTLV-2 antibody. Sufficient sera was available for seven samples which were further tested in the second Western blot assay (Diagnostic Biotechnology). These gave identical results to the Cambridge Biotech assay.

Sera from five of 194 Afro-Caribbean women born in the Caribbean were positive for HTLV-1 in contrast to only two of 596 Afro-Caribbean women born in the UK which is a 7.6-fold higher risk ($P = 0.012$). No information was available on the birth place of one HTLV-1 seropositive Afro-Caribbean woman. All eight seropositive Afro-Caribbean women had Afro-Caribbean partners.

Sera from three African antenatal attenders were positive for HTLV-1. Two of these women had been born in Africa, with no information available on the birthplace of the third clinic attender. All three women had African partners. The serum of one of 3,049 Caucasian antenatal clinic attenders was positive for HTLV-1 antibodies: This seropositive woman was born in the UK and had a Caucasian partner. Two sera contained antibodies to HTLV-2, one from a Caucasian woman who was born in the UK with a Caucasian partner, and the other from an African woman who was born in Africa with an African partner.

DISCUSSION

The modified particle agglutination test offers a relatively inexpensive method of screening large numbers of sera for HTLV antibodies and the initial reactive rate of 3.8% is similar to that observed by others [Brennan et al., 1993]. Specificity was achieved by confirmation in an ELISA followed by Western blot. This testing strategy was adopted to detect HTLV-1 infections. ELISAs based on HTLV-1 have a lower sensitivity for the detection of HTLV-2 antibodies [Nightingale et al., 1993], therefore, the identification of only two HTLV-2 infections in this study may be an underestimate. As no firm disease associations have been linked to HTLV-2, we were less concerned about identifying HTLV-2 in-

TABLE II. Demographic Data on 12 Sera Positive for HTLV-1 Antibody

Ethnicity	Birth place	No. HTLV-1 positive	Rate of HTLV-1/ 10,000 sera[a]
Caucasian	UK	1	3.3 (0.6–18)
Afro-Caribbean	Caribbean	5	
Afro-Carribean	UK	2	97 (42–190)
Afro-Caribbean	No information	1	
African	Africa	2	26 (5.5–78)
African	No information	1	

[a]Rate by ethnicity, irrespective of birth place (95% confidence limits).

fections. However, US guidelines state that such patients should be counselled and advised against breast feeding [Anon, 1993]. The modified gel agglutination test, although suitable for retrospective epidemiological studies, may be less appropriate for prospective screening given that this is an in house modification of a commercial assay and would therefore require rigorous quality control. The HTLV European Research Network recommends screening using a simple sensitive assay, such as the particle agglutination test, followed by confirmation using a more specific ELISA and Western blotting [Weber and Taylor, 1996].

The overall rate of HTLV-1 prevalence in antenatal attenders of 0.19% is similar to rates of 0.21, 0.26, and 0.14% observed in similar populations by others [Tosswill et al., 1990; Banatvala et al., 1990; Nightingale et al., 1993]. The prevalence of HTLV-1 carriage in Caucasian women was 0.033% which is higher than the rate of 0.005% found in North London blood donors, a predominantly Caucasian population [Brennan et al., 1993]. Similar differences have been observed for other viral infections, such as hepatitis B virus and HIV, reflecting the self selection of blood donors. The higher prevalence, of about 1 per 400, in African women has been observed by others [Tosswill et al., 1990; Banatvala et al., 1990], and is due to the higher level of HTLV-1 endemicity in Africa. The majority of this group were born in Africa and had African partners.

The highest prevalence of HTLV-1 was observed in Afro-Caribbeans, and those born outside the UK were at greater risk of HTLV-1 carriage than Afro-Caribbean women born in the UK. In this study this difference reaches statistical significance although there are two potential confounders, age and the possibility that an HTLV-1 positive woman attended the antenatal clinic more than once during the study period. In HTLV-1 endemic areas seropositivity increases with increasing age. This is particularly true of women as sexual transmission is more efficient from male to female than from female to male [Kajiyama et al., 1986]. In addition Tosswill and colleagues noted that Afro-Caribbean women born in the Caribbean were on average 6.6 years older than those born in the UK [Tosswill et al., 1990]. In this study we did not collect data on age and although we would expect those born in the Caribbean to be slightly older, it is unlikely that this would account for the observed difference in HTLV-1 prevalence. During this 20 month study it is possible that a number of women may have attended the antenatal clinic on more than one occasion. The re-attendance of HTLV1 positive women may have resulted in bias. This is a potential confounder in all studies where duplicates are not removed prior to anonymisation. The reasons for the different prevalence between first and second generation Afro-Caribbeans are unclear but could relate to breast feeding practice. A vertical transmission rate of 38% has been reported in Japan [Hino, 1989]. However, as the majority of HTLV-1 infections are thought to be sexually acquired [Blattner et al., 1986], breast feeding may not be the only factor responsible for this difference.

With an overall HTLV-1 positivity rate of one per 500, the cost of antenatal screening to identify each HTLV-1 positive woman can be estimated at £5,000 (using a test cost of £10, which includes confirmation tests). If the vertical transmission rate of HTLV-1 is assumed to be 20% then the cost to prevent a single HTLV-1 transmission would be £25,000. However, the introduction of HTLV screening into laboratories already undertaking universal antenatal rubella or hepatitis B surface antigen screening would incur only marginal costs. Assuming a marginal test cost of £2.50 the figure for preventing one HTLV-1 transmission would fall to £6,250. Selective screening of African and Afro-Caribbean women, with a combined prevalence of HTLV-1 of 1 in 180, would prevent a single HTLV-1 transmission at the cost of £2,250. A selective screening policy rather than universal screening would appear more attractive in areas with relatively high HTLV-1 prevalence but would probably miss the majority of HTLV-1 infections in areas of low prevalence. However, a full cost-benefit analysis would need to include costs of counselling, the morbidity and mortality of infections and disease prevented. Brennan estimated the cost of preventing HTLV associated disease in a recipient's lifetime by screening of donor blood to be £1.3 million [Brennan et al., 1993]. Assuming the same rate of HTLV-associated disease in this population, selective screening of our antenatal population would result in disease prevention at a much lower cost of about £100,000 per case (cost of prevention £2,250 vs. £30,000 for screening of blood donors). This amount is probably similar to the costs of care incurred by HTLV induced disease. While selective screening of blood donors is thought to be inefficient and the debate on universal testing continues [Dalgleish, 1993; Pagli-

uca et al., 1995], this does not appear to be the case for selective screening in antenatal clinics with a high proportion of African and Afro-Caribbean attendants. In our a study such a policy would have detected 11 of the 12 HTLV carriers and would have been cost neutral. With the expansion of universal testing of antenatal women for HIV infection and the likely development of assays which detect both HIV and HTLV antibodies the current situation may change, allowing for more cost-effective antenatal screening of HTLV infections.

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